Policy and template language for safety and event reporting

Approved by HSRAC on: September 30, 2013
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The NIH has recently approved new reporting requirements for adverse events and protocol deviations, as outlined in SOP 16, "Reporting Requirements for Unanticipated Problems, Adverse Events and Protocol Deviations." (This document can be found at https://federation.nih.gov/ohsr/nih/index.php). Protocols that are not compliant with this new policy should ultimately be amended. However, to avoid overwhelming the IRBs with amendments, the following Appendix has been approved by the Office of General Counsel and the Human Subjects Research Advisory Committee to immediately supersede any protocol text on reporting of these events.

This Appendix will apply to all ongoing studies until the necessary reporting requirements have been integrated into the protocol by an IRB-approved amendment. Researchers may request amendments for various waivers (suggested approved text also below) or for other protocol-specific requirements. All protocols should be revised to reflect the new Appendix text at the time of Continuing Review, or with the next IRB action.

Instructions: All protocols should include the standard language in section 1 below, "Appendix: Event Characterization and Reporting to the IRB, Clinical Director (CD), and (as applicable) Sponsor". Use section 2 below to request waivers from reporting to the IRB certain: minor protocol deviations, adverse events, and/or deaths. Use section 3 to alter or waive reporting non-UP deaths to the CD. (Instructional language, blue text is to be updated as appropriate for each study and paragraph numbering should be stripped prior to amending a protocol.)

1. Text to apply to all protocols until the protocol is amended:

APPENDIX [add letter, number as applicable] – Event Characterization and Reporting to the IRB, Clinical Director (CD), and (as applicable) Sponsor

Approved by HSRAC on [**DATE**]

This appendix is in force until the protocol reporting requirements have been amended and approved by the IRB.

Adverse events, protocol deviations, unanticipated problems (UP), Unanticipated Adverse Device Effects (UADEs), serious adverse events, sponsor and serious, are defined as described in NIH HRPP SOP 16 ("Reporting Requirements for Unanticipated Problems, Adverse Events and Protocol Deviations."). All adverse events occurring during the study, including those observed by or reported to the research team, will be recorded. Serious unanticipated problems, Unanticipated Adverse Device Effects and serious protocol deviations, will be reported to the

IRB and CD as soon as possible but not more than 7 days after the PI first learns of the event. Not serious unanticipated problems will be reported to the IRB and CD as soon as possible but not more than 14 days after the PI first learns of the event. Not serious protocol deviations will be reported to the IRB as soon as possible but not more than 14 days after the PI first learns of the event.

Deaths will be reported to the Clinical Director within 7 days after the PI first learns of the event.

[The following will apply to FDA-regulated protocols, as applicable]

[For drugs or biologics:] The PI will immediately report SAEs to the Sponsor according to the requirements of 21 CFR 312.64(b) and as agreed upon with the sponsor. The PI will record nonserious AEs and report them to the Sponsor according to the timetable for reporting specified in the protocol (21 CFR 312.64(b)).

[For devices:] The PI will report UADEs to the Sponsor as soon as possible, but no more than 10 working days after the PI first learns of the event. For IDE research, the PI will report deviations from the investigational plan that were intended to protect life or physical well-being of a subject in an emergency to the Sponsor and IRB within 5 days.

2. Waiver of Reporting to the IRB of anticipated minor protocol deviations, adverse events and deaths due to underlying disease or population under study unless determined to be an Unanticipated Problem

Instructions: Use the text below within protocol amendments if requesting a waiver from reporting as allowed by SOP 16. Add protocol-specific text in place of blue text below.

- ***For waiver of Reporting to the IRB of anticipated minor protocol deviations***

  [To request that the IRB waive reporting to the IRB about anticipated minor protocol deviations except if they become a UP, insert the following language:] The following anticipated minor deviations in the conduct of the protocol will not be reported to the IRB unless they occur at a rate greater than that which is anticipated to occur: [list specific deviation and rate, e.g., *a single missed time-point for blood draw in the XX test, which occurs in about 5% of tests and does not compromise the integrity of the data*]. If the rate of these events exceeds the rate specified by the protocol, the events will be classified and reported as though they are Unanticipated Problems.

- ***For waiver of Reporting to the IRB of anticipated adverse events:***

  [To request that the IRB waive reporting to the IRB about anticipated adverse events except if they become a UP, insert the following language:] The following anticipated

non-UP adverse events will not be reported to the IRB unless they occur at a rate greater than that known to occur in this [condition or population, specify]: [list specific adverse events here, e.g., hypokalemia, and rate]. If the rate of these events exceeds the rate specified in the protocol [or investigator's brochure (if applicable)], the events will be classified and reported as though they are Unanticipated Problems. [And/or insert:] The following anticipated non-UP adverse events will not be reported to the IRB unless they occur at a severity greater than that known to occur in this condition: [list specific adverse event and severity, e.g hypokalemia < 3.0 mEq/L].

- ***For waiver of Reporting to the IRB of anticipated adverse events on an FDA-regulated trial:***

  [A waiver of reporting to the IRB must not be contrary to the Sponsor agreement. To request that the IRB waive reporting to the IRB about anticipated adverse events, related to an IND agent, except for when they become a UP, insert the following language:] The following anticipated adverse events will not be reported to the IRB unless they occur at a rate or severity greater than that known to be associated with [list IND agent(s)]. Examples of expected adverse events include but are not limited to those events detailed in the Investigator's Brochure for [IND agent] and in the protocol's risk section, [as well as xxxxx]. The waivers that apply here are: [include the severity and rate in the protocol's risk section if they are not in the Investigator's Brochure, e.g hypokalemia > 3.0 mEq/L or in < 50% of subjects.] If the rate or severity of these events exceeds the rate or severity anticipated in the protocol or investigator's brochure, the events will be classified and reported as though they are Unanticipated Problems.

- ***For waiver of Reporting to the IRB of deaths based on the natural history of the disorder or population under study:***

  [To request that the IRB waive reporting to the IRB about deaths based on the natural history of the disorder or population, insert the following language:] The following anticipated deaths based on the natural history of the disorder or population under study will be reported to the IRB only if they occur at a rate greater than that known to occur in this [condition or population, specify], which is XX% of subjects: [add specific waiver language here, e.g., death from myocardial infarction]. If the rate of these deaths exceeds the rate anticipated in the protocol [or investigator's brochure (as applicable)], the events will be classified and reported as though they are Unanticipated Problems.

For waiver of reporting non-UP deaths to the CD

Instructions: Append this to the CD reporting criteria for deaths:

Deaths will be reported to the Clinical Director within 7 days after the PI first learns of the event. [This requirement may be waived or altered by the CD. If reporting of deaths to the CD is waived by the CD, do not insert the language above. If it is altered by the CD, insert the relevant language instead of the language above.]